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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/737,476	12/18/2000	Leo G.J. Frenken	P 0275850 T 7060C	9341

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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/737,476	FRENKEN ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *8 and 10-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed January 23, 2004 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 3, 2003 has been entered.

Claims 1-2, 4-6, 9 and 14 are currently amended.

Claims 8 and 10-13 are withdrawn.

Claims 1-14 are pending.

Claims 1-7, 9 and 14 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 102

Claims 1, 3, 7, 9 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Magnuson et al. (Protein Expression and Purification, 1996, Vol. 7, pages 220-228).

The claims are drawn to a method for modifying a plant to produce an antibody in a cellular compartment comprising introducing into a plant a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain, said sequence being operably linked to one or more promoters and said sequence further comprising an additional sequence

encoding a peptide sequence capable of targeting said antibody to said cellular compartment, and expressing the antibody which is devoid of light chain domains but capable of specific binding with an antigen, in a cellular compartment. The claims are also drawn to plants obtained by said method or comprising said DNA sequence.

Magnuson et al. teach a method for modifying a plant to produce an antibody comprising introducing into tobacco suspension culture cells a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain and obtained from a 93G7 monoclonal antibody, said sequence being operably linked to a CaMV 35S promoter, and expressing the antibody which is devoid of light chain domains but capable of specific binding with an antigen, in the cytoplasm and plasma membrane (page 222 Figure 1; page 223 Table 1 and Figures 2-3; page 224 Figures 4-5; page 225 Table 2; page 226 Figure 9). The DNA sequence taught by Magnuson et al. further comprises an additional sequence encoding a native leader peptide sequence capable of targeting said antibody to the cytoplasm and plasma membrane (page 224 column 1 first paragraph).

Claims 1, 2, 7, 9 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Casterman et al. (WO 94/04678, 3 March 1994, Applicant's IDS), for the reasons of record set forth in the office action mailed June 3, 2003.

Applicant's arguments filed December 3, 2003, have been fully considered but they are not persuasive.

Applicants argue that a mere reference in a cited reference to another article that teaches bits and pieces of items required to practice the claimed invention does not necessarily enable the

cited reference. Applicants also assert that extra references may only be relied upon to show the enablement of a primary reference where the claimed composition or machine disclosed is identical. Applicants additionally assert that the applied reference of Casterman et al. is presumed operable until Applicants rebut that presumption, and in rebuttal Applicants argue that one skilled in the art would have no reason to express the immunoglobulins of Casterman et al. in plants based solely on Hiatt et al., because there was no reasonable expectation of success in view of the difficulties of heavy chain expression in plants as demonstrated in the prior art, for example by the disclosures of Ma et al. and the Vu PhD thesis, both of record. (reply pages 8-9)

The Office maintains that the cited reference of Casterman et al. is enabled. The Hiatt et al. reference cited in Casterman et al. does not teach bits and pieces of items required to practice the claimed invention. The Hiatt et al. reference cited in Casterman et al. would in fact anticipate the rejected claims but for the requirement of claim 2 that the heavy chain immunoglobulin be obtained from camelids, and but for the silence of Hiatt et al. with respect to whether their expressed heavy chain immunoglobulin is capable of specific binding with an antigen. Furthermore, Applicants' observation that Ma et al. and the Vu PhD thesis teach that expression of heavy chains in plants is not straightforward is not germane to the instant rejection, since the claims are rejected as being anticipated under 35 USC 102 rather than as obvious under 35 USC 103, and since Hiatt et al. in fact successfully introduced into a plant and expressed a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain (Hiatt et al., Nature, 1989, Vol. 342, pages 76-79, see page 77 Table 1 and Figure 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over either of Magnuson et al. (Protein Expression and Purification, 1996, Vol. 7, pages 220-228) or Casterman et al. (WO 94/04678, 3 March 1994, Applicant's IDS), in view of Owen et al. (Biotechnology, Vol. 10, pages 790-794, July 1992).

The claim is drawn to a method for modifying a plant to produce an antibody comprising introducing into a plant a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain, said sequence being operably linked to one or more promoters, and expressing the antibody which is devoid of light chain domains but capable of specific binding with an antigen that is a protein present in a plant, in a cellular compartment.

The teachings of Magnuson et al. are set forth above in the rejection of claims 1, 3, 7, 9 and 14 under 35 USC 102.

The teachings of Casterman et al. are set forth in the rejection of claims 1 and 2 under 35 USC 102 at pages 11-12 of the Office action mailed September 10, 2002.

Neither Magnuson et al. nor Casterman et al. teach the expression in plants of a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain but capable of specific binding with an antigen that is a protein present in a plant.

Owen et al. teach the expression in plants of a DNA sequence encoding a single-chain Fv recombinant immunoglobulin capable of specific binding with an antigen that is a phytochrome protein present in a plant, as set forth previously in the rejection of claims 1, 3, 4, 7 and 9 under 35 USC 102 at pages 8-9 of the Office action mailed September 10, 2002.

Given the success of Magnuson et al. in expressing in a plant a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain but capable of specific binding with an antigen or the teaching of Casterman et al. to do the same, and given the success of Owen et al. in expressing in a plant a DNA sequence encoding a single-chain Fv recombinant immunoglobulin capable of specific binding with an antigen that is a phytochrome protein present in a plant, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to express in a plant any type of immunoglobulin capable of specific binding with an antigen that is a protein present in a plant, including a heavy chain immunoglobulin devoid of a variable light chain domain, for the purpose of manipulating a plant's physiologic responses, without any surprising or unexplained results. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over either of Magnuson et al. (Protein Expression and Purification, 1996, Vol. 7, pages 220-228) or

Casterman et al. (WO 94/04678, 3 March 1994, Applicant's IDS), in view of Le Gall et al. (Applied and Environmental Microbiology, Vol. 64, No. 11, pages 4566-4572, November 1998).

The claim is drawn to a method for modifying a plant to produce an antibody comprising introducing into a plant a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain, said sequence being operably linked to one or more promoters, and expressing the antibody which is devoid of light chain domains but capable of specific binding with an antigen that is a plant or animal pathogen, in a cellular compartment.

The teachings of Magnuson et al. are set forth above in the rejection of claims 1, 3, 7, 9 and 14 under 35 USC 102.

The teachings of Casterman et al. are set forth in the rejection of claims 1 and 2 under 35 USC 102 at pages 11-12 of the Office action mailed September 10, 2002.

Neither Magnuson et al. nor Casterman et al. teach the expression in plants of a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain but capable of specific binding with an antigen that is a plant or animal pathogen.

Le Gall et al. teach the expression in plants of a DNA sequence encoding a single-chain Fv recombinant immunoglobulin capable of specific binding with an antigen that is a stolbur phytoplasma plant pathogen, as set forth previously in the rejection of claims 1, 3, 4, 5 and 7 under 35 USC 102 at pages 10-11 of the Office action mailed September 10, 2002.

Given the success of Magnuson et al. in expressing in a plant a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain but capable of specific binding with an antigen or the teaching of Casterman et al. to do the same, and given the success of Le Gall et al. in expressing in a plant a DNA sequence encoding a single-chain Fv

recombinant immunoglobulin capable of specific binding with an antigen that is a stolbur phytoplasma plant pathogen, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to express in a plant any type of immunoglobulin capable of specific binding with an antigen that is a plant pathogen, including a heavy chain immunoglobulin devoid of a variable light chain domain, for the purpose of improving a plant's resistance to infection by a plant pathogen, without any surprising or unexplained results. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over either of Magnuson et al. (Protein Expression and Purification, 1996, Vol. 7, pages 220-228) or Casterman et al. (WO 94/04678, 3 March 1994, Applicant's IDS), in view of Artsaenko et al. (The Plant Journal, Vol. 8, No. 5, pages 745-750, 1995).

The claim is drawn to a method for modifying a plant to produce an antibody comprising introducing into a plant a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain, said sequence being operably linked to one or more promoters, and expressing the antibody which is devoid of light chain domains but capable of specific binding with an antigen that is a plant hormone or metabolite, in a cellular compartment.

The teachings of Magnuson et al. are set forth above in the rejection of claims 1, 3, 7, 9 and 14 under 35 USC 102.

The teachings of Casterman et al. are set forth in the rejection of claims 1 and 2 under 35 USC 102 at pages 11-12 of the Office action mailed September 10, 2002.

Neither Magnuson et al. nor Casterman et al. teach the expression in plants of a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain but capable of specific binding with an antigen that is a plant hormone or metabolite.

Artsaenko et al. teach the expression in plants of a DNA sequence encoding a single-chain Fv recombinant immunoglobulin capable of specific binding with an antigen that is an abscisic acid plant hormone, as set forth previously in the rejection of claims 1, 3 and 6-7 under 35 USC 102 at pages 9-10 of the Office action mailed September 10, 2002.

Given the success of Magnuson et al. in expressing in a plant a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain but capable of specific binding with an antigen or the teaching of Casterman et al. to do the same, and given the success of Artsaenko et al. in expressing in a plant a DNA sequence encoding a single-chain Fv recombinant immunoglobulin capable of specific binding with an antigen that is an abscisic acid plant hormone, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to express in a plant any type of immunoglobulin capable of specific binding with an antigen that is a plant hormone, including a heavy chain immunoglobulin devoid of a variable light chain domain, for the purpose of manipulating a plant's physiologic responses, without any surprising or unexplained results. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins  4/2/04